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14. ABSTRACT The goal of the project is to define the clinical phenotype of late-life dementia in veterans who have been exposed to TBI. Our hypothesis is that TBI in early to mid-life is associated with a dementia phenotype that has features distinguishable from AD. In the first year, we completed the screening survey portion of the study and found that over half of the veterans surveyed (n=289) had a history of head injury, with over 20% requiring hospitalization. Compared to those without TBI, those with TBI had higher levels of depression (61.3% for hospitalization group vs. 55.3% for head injury symptom group vs. 24.2% for non-TBI group, P<0.001) and PTSD (37.1% for hospitalization group vs. 21.4% head injury symptoms group vs. 8.1% for non-TBI group, P<0.001). We also found that TBI is associated with a higher history of psychiatric disorders and current cognitive symptoms. A manuscript based on these results is in preparation. Data is currently being collected for the cross-sectional study phase of the project. The results will determine if a clinical phenotype of dementia in individuals with TBI exists, which has relevance for future treatment.					
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Introduction

One of the most feared long-term consequences of traumatic brain injuries (TBIs) is dementia. TBI in early and mid-life is associated with an increased risk of late-life dementia, with relative risks in the order of 2.5 to 5.0 (1-3). Military veterans are at high risk of TBI during combat as well as during peacetime service (4). The goal of this project is to define the clinical phenotype of late-life dementia in veterans who have been exposed to TBI. Our hypothesis is that TBI in early to mid-life is associated with a dementia phenotype that has features distinguishable from Alzheimer's disease (AD). Specifically, we hypothesize that: (1) veterans with TBI-associated cognitive impairment or dementia will have higher levels of symptoms of depression, anxiety, and Parkinsonism compared to veterans with cognitive impairment/dementia who have not experienced a TBI, and (2) veterans with TBI-associated cognitive impairment or dementia will have prominent deficits in executive function, compared to veterans with cognitive impairment/dementia who have not had a TBI. This 18-month, cross-sectional study will lead to a better understanding of the features of TBI-associated dementia in retired military veterans. The project will develop clinical criteria to allow accurate and early diagnosis and is critically important to the Department of Defense, the Veterans Administration, as well as to society at large.

Body

Task 1: Screen retired military service men and women at each site [Armed Forces Retirement Home (AFRH), Washington, DC and Veterans Home of California-Yountville (VHC-Yountville)]

Subtask 1a. Planning and Regulatory Review

In the first two quarters of the project we received full regulatory approval for both sites. The California site had two separate protocols approved. For the screening survey, the protocol titled "Prevalence of Traumatic Brain Injury, Memory Problems, and Post Traumatic Stress in Retired Military Servicemen and Women" received University of California, San Francisco (UCSF) Committee on Human Research (CHR) approval on June 20, 2012. This protocol was reviewed and approved by the US Army Medical Research and Material Command (USAMRMC), Office of Research Protection (ORP), and Human Research Protection Office (HRPO), and received final approval on February 4, 2013. The protocol received continuing renewal approval from UCSF on May 22, 2013 and the official continuing review report was submitted to USAMRMC HRPO. "Endophenotypes of Dementia Associated with Traumatic Brain Injury in Retired Military Personnel", the cross-sectional study protocol, received UCSF CHR approval on October 11, 2012 and USAMRMC, ORP, and HRPO approval on February 4, 2013. The protocol received continuing renewal approval from UCSF on October 4, 2013 and the official continuing

review report was submitted to USAMRMC HRPO. The sub-site Uniformed Services University of the Health Sciences (USUHS) received approval for the combined survey and study protocol “Endophenotypes of Dementia Associated with Traumatic Brain Injury in Retired Military Personnel” from the USUHS Institutional Review Board on March 20, 2013. USAMRMC, ORP, and HRPO second level approval was received for the sub-site on April 17, 2013.

The subcontract with the Henry Jackson Foundation (HJF) was executed on January 30, 2013. Once the grant was awarded, we initiated monthly conference calls with the sub-site to discuss study initiation and progress as well as refining the study protocol, measurements, operations manual, and study survey. Please see the appendix for a copy of the survey. Both sites held meetings with administrators at the VHC-Yountville and AFRH to discuss study set-up and logistics. Once the screening survey was underway, our monthly conference calls focused on writing and refining the case report forms, order of tests, and manual of operations for the second phase of the study. Dr. Kramer trained all study personnel on the administration of the neuropsychological tests; Dr. Kramer traveled to HJF and select HJF study staff traveled to UCSF for training.

Subtask 1b. Screen retired service members at AFRH and VHC-Yountville

Data collection for the survey screening portion of the study (Phase 1) is complete. Approximately one-third of individuals residing in independent living at VHC-Yountville and AFRH completed surveys for a combined total of 298. Eighty-four percent of survey participants were white; 90% were male, and the mean age was 78.5 years \pm 10.7. TBI exposure was defined as head injury resulting in symptoms (including being dazed, amnesia for the injury, memory gaps, loss of consciousness) or subsequent hospitalization. Current post-traumatic stress disorder (PTSD) symptoms were assessed using the PTSD-2 Checklist (PCL-2). Participants reported lifetime presence of psychiatric diagnoses and current severity of subjective memory complaints, and completed objective cognitive orientation items.

TBI with head injury symptoms only was found in 34.6% (n = 103); 20.8% (n = 62) had TBI with subsequent hospitalization. 26.8% had military TBI; almost 50% had civilian TBI; and 13.4% had both military and civilian TBI (see Table 1 below). Table 2 shows the baseline characteristics of participants in each of the TBI groups.

Table 1. Prevalence of TBI groups and head injury symptoms.

	Any cause*, N (%)	Military, N (%)	Civilian, N (%)
<i>Exposure to head injury</i>			
None or head injury without symptoms	124 (41.6)	218 (73.2)	150 (50.3)
TBI with only head injury symptoms	103 (34.6)	42 (14.1)	95 (31.9)
TBI with subsequent hospitalization	62 (20.8)	20 (6.7)	48 (16.1)
<i>Head injury symptoms</i>			
Dazed, confused, seeing stars	136 (45.6)	52 (17.4)	114 (38.3)
Not remembering the injuries	55 (18.5)	15 (5.0)	46 (15.4)
Memory gaps	63 (21.1)	23 (7.7)	50 (16.8)
Duration of LOC	90 (30.2)	31 (10.4)	72 (24.2)
<30 mins	51 (17.1)	13 (4.4)	33 (11.1)
30 mins-24hrs	10 (3.4)	5 (1.7)	7 (2.3)
24 hrs+	12 (4.0)	2 (0.7)	12 (4.0)
Unknown duration	25 (8.4)	11 (3.7)	22 (7.4)

*If subjects had both civilian and military TBI of differing severity, the more severe category was used for TBI status.

%'s based on total number of participants, 298. Completed responses $n = 281-294$.

LOC = loss of consciousness.

Table 2. Baseline Characteristics by TBI Status.

Characteristics mean \pm SD, N (%)	No TBI* (n = 124)	TBI with symptoms (n = 103)	TBI with hospitalization (n = 62)	P-value for trend
Age, years	81.2 (9.1)	78.0 (10.1)	75.1 (12.1)*	0.001
Male gender	105 (84.7)	97 (94.2)*	59 (95.2)*	0.006
White	98 (79.0)	89 (86.4)	54 (87.1)	0.44
Currently married	13 (10.5)	16 (15.5)	9 (14.5)	0.46
Education (> high school)	56 (45.2)	59 (57.3)	33 (53.2)	0.19
Military service, years	12.1 (8.9)	7.0 (7.6)*	7.3 (7.3)*	<0.001
Junior enlisted rank (E1-E4)	28 (22.6)	43 (41.7)*	29 (46.8)*	0.005
Any military injury	36 (29.0)	61 (59.2)*	36 (58.0)*	<0.001

*P < 0.05 when compared to non-TBI group as per post-hoc analyses.

Compared to those without TBI, those with TBI had higher levels of depression (61.3% for hospitalization group vs. 55.3% for head injury symptom group vs. 24.2% for non-TBI group, $P < 0.001$) and PTSD (37.1% for hospitalization group vs. 21.4% head injury symptoms group vs. 8.1% for non-TBI group, $P < 0.001$). Figure 1 shows that individuals with TBI had more active psychiatric symptoms and were more likely to have multiple psychiatric diagnoses compared to those with no head injury. Severity of TBI was associated with higher severity scores of current

PTSD symptoms on PCL-2 (3.9 ± 2.2 for hospitalization group vs. 3.2 ± 2.0 for head injury symptom group vs. 2.7 ± 1.6 for non-TBI group, $P < 0.001$) (See Figure 2).

FIGURE 1. Severity of Psychiatric Diagnosis by TBI Status.

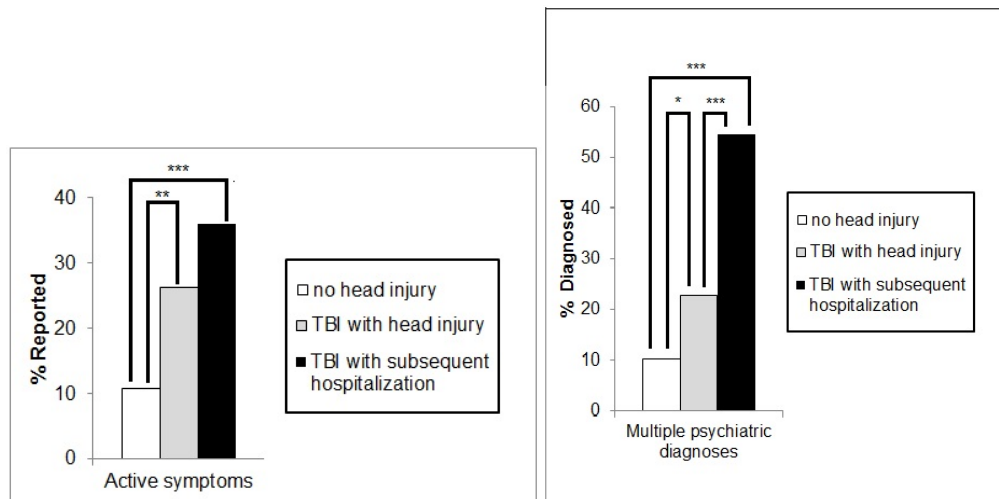
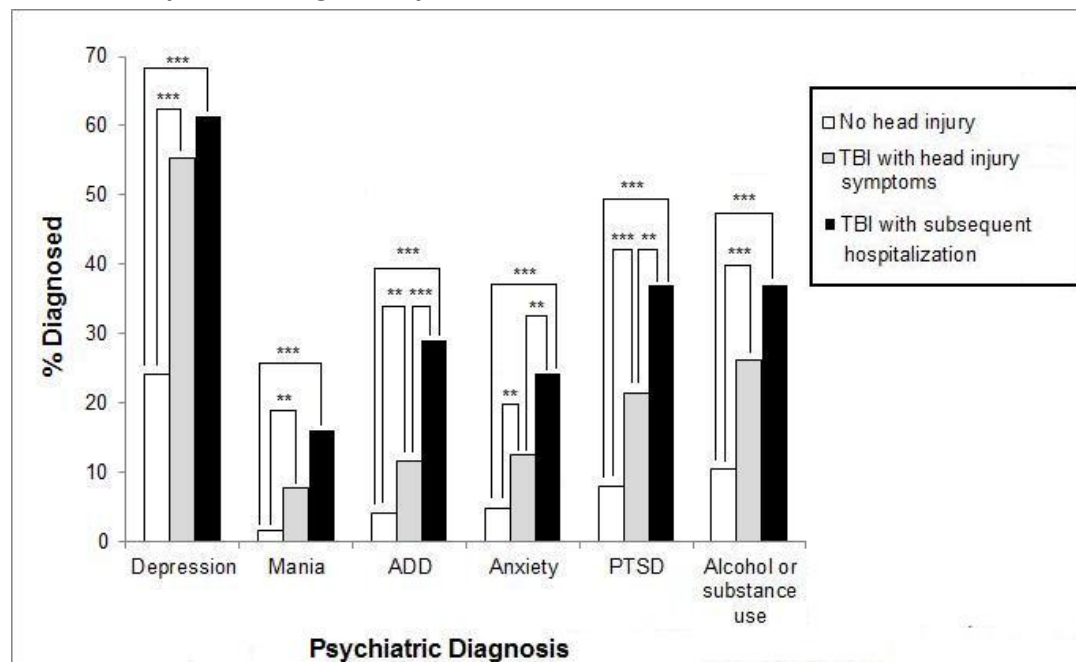


Figure 1A.

Figure 1B.

* $P < 0.10$, ** $P < 0.01$, *** $P < 0.001$

FIGURE 2. Psychiatric Diagnosis by TBI Status.



ADD = attention-deficit disorder

Post-traumatic stress disorder = PTSD

* $P < 0.10$, ** $P < 0.01$, *** $P < 0.001$

Compared to those without TBI, participants with TBI and subsequent hospitalization were more likely to have more subjective memory complaints (25.8% for hospitalization group vs. 9.7% for non-TBI, $P = 0.008$); this trended towards significance for the TBI with head injury symptom group (19.4%, $P = 0.051$). There were no significant differences in performance on orientation items ($P = 0.32$).

From the screening survey we have shown that TBI is a common occurrence in the older veterans residing in veterans homes, affecting over half of the population, and is associated with a higher history of psychiatric disorders and current cognitive symptoms. An abstract with this data was presented at the 2013 Alzheimer's Association International Conference in Boston, MA, and a manuscript describing the results will be submitted to a peer-reviewed journal by the end of 2013.

Task 2. Enroll retired service members at AFRH and VHC-Yountville

Potentially eligible participants are identified using information from: (1) the survey in which participants consented to be contacted for a future study, and (2) chart review through an IRB-approved Waiver of Authorization for Recruitment. The potentially eligible participants are contacted and asked if they are interested in taking part in the cross-sectional study. After a thorough explanation of the study and procedures, those interested in participating are scheduled for a study visit and consented before any study procedures take place. The inclusion and exclusion criteria are listed below. If, upon learning further information, the patient does not meet eligibility criteria, they are considered a screen failure and do not go through study procedures.

Inclusion Criteria

- TBI Participants:
 - Aged 50-95
 - Resident in the independent living facility at the VHC-Yountville or the AFRH-Washington D.C.
 - Can speak, read, and understand English
 - Capacity to provide consent to participate in research
 - MMSE score ≥ 20
 - History of traumatic brain injury: required to have sought medical treatment (ER visit, doctor visit, hospitalization) after a head injury
- Controls (without a history of TBI):
 - Aged 50-95
 - Resident in the independent living facility at the VHC-Yountville or the AFRH-Washington D.C.
 - Can speak, read, and understand English

- Capacity to provide consent to participate in research
- MMSE score ≥ 20
- No history of TBI or concussion (defined as no head injury resulting in being dazed, having a memory gap, loss of consciousness, or medical treatment)

Exclusion Criteria

- TBI Participants:
 - History of penetrating brain injury
 - Currently active disabling neurological or psychiatric condition (such as epilepsy, multiple sclerosis, cortical stroke, hypoxic-ischemic encephalopathy, encephalitis or schizophrenia)
 - Lack of competence to provide consent to participate in research
 - No verbal and oral fluency English
 - Non-correctable vision or hearing impairments (severe enough to impair testing)
- Controls (without a history of TBI):
 - Currently active disabling neurological or psychiatric condition (such as epilepsy, multiple sclerosis, cortical stroke, hypoxic-ischemic encephalopathy, encephalitis or schizophrenia)
 - Lack of competence to provide consent to participate in research
 - No verbal and oral fluency English
 - Non-correctable vision or hearing impairments (severe enough to impair testing)

Subtask 2a. Evaluate both cases and controls

Data collection is currently underway at both sites. Data for each participant (TBI or control) is collected over two separate appointments, each taking no longer than 90 minutes. The first visit involves signing the consent and HIPAA documents, gathering basic demographic and medical history data, various health and lifestyle questionnaires, and a neurological examination. All the neuropsychological tests take place at the second visit. As of 10/15/13 we have collected data from 20 individuals, 22 with a history of TBI requiring medical care, and 8 controls.

Key Research Accomplishments

- Regulatory review completed at both study sites.
- Working relationship established between the researchers and AFRH and VHC-Yountville.
- Screening survey developed and administered to 298 veterans.
- Survey data analyzed and manuscript currently in preparation.
- Developed operating procedures, case report forms, and study forms for cross-sectional study.
- Began data collection for cross-sectional study.

Reportable Outcomes

- Abstract was presented as a Platform Presentation at the 2013 Alzheimer's Association International Conference in Boston, MA
- Manuscript in preparation with results from screening survey study. We plan to submit to peer-review journal by end of 2013.
- Utilizing pilot data, we applied to the CENC to expand on this project in order to obtain brain pathology, expand our cohort, and follow the cohort longitudinally. Dr. Ramon Diaz-Arrastia will serve as the PI of the project with Dr. Kristine Yaffe as Co-PI. As a result of the CENC submission, Dr. David Cifu was awarded the consortium. The project we submitted was well received, and we were asked to revise our project with a potential start date of Summer 2014. There is no overlap scientifically with this project or funding overlap.

Conclusions

Over the past year we developed and administered a survey to nearly 300 veterans residing in two veterans homes. We found that TBI is a common occurrence in the older veterans residing in veterans homes, affecting over half of the population, and is associated with a greater history of psychiatric disorders and current cognitive symptoms. The study results indicate that this understudied group of older veterans is likely a fruitful population for examining TBI-related cognitive impairment.

We are currently collecting data in the second phase of our project, a cross-sectional study to examine whether there are any clinical differences between individuals with cognitive impairment with and without history of TBI. Understanding the features of dementia in retired military veterans, and developing clinical criteria to allow accurate and early diagnosis is critically important to the Department of Defense, the Veterans Administration, as well as to society at large. For service members at increased risk of AD-type neurodegeneration as a consequence of their service in combat, early recognition is essential in order to implement preventive therapies.

References

1. S. Fleminger, D. L. Oliver, S. Lovestone, S. Rabe-Hesketh, A. Giora, Head injury as a risk factor for Alzheimer's disease: the evidence 10 years on; a partial replication. *J Neurol Neurosurg Psychiatry* **74**, 857 (Jul, 2003).
2. Z. Guo *et al.*, Head injury and the risk of AD in the MIRAGE study. *Neurology* **54**, 1316 (Mar 28, 2000).
3. B. L. Plassman *et al.*, Documented head injury in early adulthood and risk of Alzheimer's disease and other dementias. *Neurology* **55**, 1158 (Oct 24, 2000).
4. S. Okie, Traumatic brain injury in the war zone. *N Engl J Med* **352**, 2043 (May 19, 2005).
5. A. V. Savonenko *et al.*, Alzheimer's therapeutics: translation of preclinical science to clinical drug development. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* **37**, 261 (Jan, 2012).
6. C. R. Jack, Jr. *et al.*, Evidence for ordering of Alzheimer disease biomarkers. *Arch Neurol* **68**, 1526 (Dec, 2011).

Name _____

Veterans Home of California Yountville Questionnaire

Please answer the following questions to the best of your ability. **You do not have to answer every question.** Please ask a research assistant for help if you would like assistance in filling out the questionnaire.

1. Age: _____

3. Gender:

- ☐ Male
☐ Female

2. Race/Ethnicity:

- ☐ Caucasian/White
☐ African American
☐ Hispanic
☐ Asian/Pacific Islander
☐ Other _____

4. Highest Level of Civilian Education:

- ☐ Some High School
☐ GED
☐ High School Diploma
☐ Associate's Degree
☐ Bachelor's Degree
☐ Master's Degree
☐ Doctorate Degree

5. Highest Grade/Rank

- ☐ E1 ☐ E7
☐ E2 ☐ E8
☐ E3 ☐ E9
☐ E4 ☐ E10
☐ E5 ☐ O1-O3
☐ E6 ☐ O4-O9

6. How many years did you serve in the military? _____

7. Which branch of the military?

- ☐ Navy
☐ Army
☐ Air Force
☐ Marines
☐ Coast Guard
☐ National Guard

8. What is your current marital status?

- ☐ Single, never married
☐ Married, living with spouse
☐ Married, but separated
☐ Married, geographically separated
☐ Divorced
☐ Widowed

9. How many times during your military service did you deploy for more than 30 days to any of the following? MARK ALL THAT APPLY

	Never	One Time	Two Times	Three or more Times
Afghanistan (OEF)/Iraq (OIF)				
Bosnia/Kosovo (Peacekeeping)				
Persian Gulf War				
Vietnam				
Korea				
WWII				
Other: _____				

10. What was your role while deployed? _____

11. During your deployments, how often were you in serious danger of being injured or killed?

- ☐ Never
☐ Once or twice
☐ Sometimes
☐ Many times

12. During your deployments, how many times did you engage the enemy in a firefight?

- ☐ Never
☐ Once or twice
☐ Sometimes
☐ Many times

13. During your DEPLOYMENTS, were you ever injured from any of the following?

Blast/explosion (IED, RPG, mortar, artillery)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Bullet	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Fragments/shrapnel	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Fall	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Friendly Fire	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Vehicle Accident	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Other, specify: _____	<input type="checkbox"/> Yes	<input type="checkbox"/> No

14. Did any injury you received during your DEPLOYMENTS involve the following?

Injury to your head	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Being dazed, confused, or "seeing stars"	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Not remembering the injury	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Have gaps in memory around the time of injury (either before or after)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Losing consciousness (knocked out)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
If yes, approximately how many minutes were you knocked out? _____		

15. Did you spend one or more nights in a hospital as a patient during your DEPLOYMENTS?

- ☐ No
☐ Yes, reason: _____

16. Do you have any metal in your body (like shrapnel, bullets or implants)? ☐ Yes ☐ No

17. Have you ever boxed? ☐ Yes ☐ No

If yes, were you ever knocked out or have a TKO? ☐ Yes ☐ No

18. Have you ever played football? ☐ Yes ☐ No

If yes, for how many years? _____

19. Anytime during your LIFE (outside of a deployment), have you ever suffered an injury to your head from any of the following?

Car or Motorcycle Accident	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Fall	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Assault or Fight	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Sports	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Other, specify: _____	<input type="checkbox"/> Yes	<input type="checkbox"/> No

20. Did the injury to your head cause any of the following:

Being dazed, confused, or "seeing stars"	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Not remembering the injury	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Have gaps in memory around the time of injury (either before or after)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Losing consciousness (knocked out)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
If yes, approximately how many minutes were you knocked out? _____		

21. Did you spend one or more nights in a hospital as a patient from having an injury to your head (not related to a deployment)?

☐ No

☐ Yes, reason: _____

22. Did you ever in your life have any of the following behavioral or emotional health problems or has a doctor ever diagnosed you with these problems?

Depression	<input type="checkbox"/> Yes	<input type="checkbox"/> No	Anxiety attacks or panic attacks	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Attention deficit disorder (ADD) or other serious problems with attention, impulsivity, or hyperactivity	<input type="checkbox"/> Yes	<input type="checkbox"/> No	Post-traumatic stress disorder (PTSD)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Problems controlling your anger	<input type="checkbox"/> Yes	<input type="checkbox"/> No	Other problems with anxiety (e.g. serious problems with nerves, worries, or fears)	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Manic-depression, mania, or bipolar disorder	<input type="checkbox"/> Yes	<input type="checkbox"/> No	Alcohol or drug problems	<input type="checkbox"/> Yes	<input type="checkbox"/> No

23. Are any of the above problems active now? ☐ Yes ☐ No

24. Below is a list of reactions that veterans sometimes experience following deployment or in response to other stressful life experiences. How often in the past 30 days did you experience the following reactions?

	Not at all	A little bit	Moderately	Quite a bit	Extremely
You had repeated, disturbing memories, thoughts, or images of a stressful experience					
You had repeated, disturbing dreams of a stressful experience					
You suddenly acted or felt as if a stressful experience were happening again (as if you were re-living it)					
You felt very upset when something reminded you of a stressful experience					
You had physical reactions (like heart pounding, trouble breathing, sweating) when something reminded you of a stressful experience					
You avoided thinking about or talking about a stressful experience or avoided having feelings about it					
You avoided activities or situations because they reminded you of one of your stressful experiences					
You had trouble remembering important parts of one of your stressful experiences					
You had a loss of interest in activities you used to enjoy					
You felt emotionally numb or unable to have loving feelings for those close to you					
You felt as if the future would somehow be cut short					
You had trouble falling asleep, staying asleep, or waking too early					
You felt irritable or had angry outbursts					
You had difficulty concentrating					
You were "super alert" or watchful or on guard					
You felt jumpy or were easily startled					

25. What stressful experience were you thinking about when you answered question 24 above?

26. How difficult have the above problems made it for you to do your work, take care of things at home, or get along with other people?

- ☐ Not at all difficult
☐ Somewhat difficult
☐ Very difficult
☐ Extremely difficult

27. At any time during your life PRIOR TO THE PAST MONTH have you been bothered (for at least one month) by any of the problems listed above in question 24 that were reactions to life experiences? Think about the most serious event.

- ☐ If Yes → Continue with question 28
☐ If No → Skip to question 31

28. Think of the one month in your life when you had the largest number of reactions associated with a highly stressful experience. During that month, how often did you have each of the following reactions?

	Not at all	A little bit	Moderately	Quite a bit	Extremely
You had repeated, disturbing memories, thoughts, or images of a stressful experience					
You had repeated, disturbing dreams of a stressful experience					
You suddenly acted or felt as if a stressful experience were happening again (as if you were re-living it)					
You felt very upset when something reminded you of a stressful experience					
You had physical reactions (like heart pounding, trouble breathing, sweating) when something reminded you of a stressful experience					
You avoided thinking about or talking about a stressful experience or avoided having feelings about it					
You avoided activities or situations because they reminded you of one of your stressful experiences					
You had trouble remembering important parts of one of your stressful experiences					
You had a loss of interest in activities you used to enjoy					
You felt emotionally numb or unable to have loving feelings for those close to you					
You felt as if the future would somehow be cut short					
You had trouble falling asleep, staying asleep, or waking too early					
You felt irritable or had angry outbursts					
You had difficulty concentrating					
You were "super alert" or watchful or on guard					
You felt jumpy or were easily startled					

29. About how old were you the very first time you had reactions like those in question 28?

(Your best estimate is fine if you cannot remember your exact age.)

- ☐ <19 ☐ 30 – 39 ☐ 50 – 59 ☐ 70 – 79
☐ 20 – 29 ☐ 40 – 49 ☐ 60 – 69 ☐ >80

30. About how many different years in your life did you have reactions like those in question 28, lasting longer than one month, associated with any of the highly stressful experiences you have ever had? (Your best estimate is fine.)

- ☐ 0 Years
☐ 1-2 Years
☐ 3-9 Years
☐ 10-19 Years
☐ 20-29 Years
☐ 30+ Years

31. Are you currently experiencing any of the following:

	Never	Rarely	Sometimes	Most of the Time
Have trouble remembering the names of people you know well?				
Have trouble remembering doctor's appointments or other commitments?				
Have trouble in conversations either coming up with the right words or understanding what others are saying?				
Have trouble using household appliances such as a TV set, microwave, or telephone?				
Get lost going to familiar places (like the grocery store)?				

32. What is the date today? _____

33. What is the name of this city? _____

34. What season is it? _____

35. How long have you lived at the Veterans Home of California-Yountville? _____

36. Did you fill this form out by yourself? ☐ Yes ☐ No

37. Would you be interested in volunteering for a brain research study about military retirees? It would take 4-6 hours of your time each year.

☐ Yes ☐ No

Thank you for taking the time to fill out this questionnaire. Please return it to a research team member or to the box located by the research team.